A Synthesis of 1-*O*-Octadec-*cis*-1′-enyl-L-glycerol

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An exchange reaction between octadecanal dimethyl acetal and D-(glycerol 1,2-carbonate) gave octadecanal di-D-(glycerol 1,2-carbonate) acetal which was converted into 3-*O*-(1-chlorooctadecyl)-D-glycerol 1,2-carbonate by the action of acetyl chloride at room temperature. The chloro-ether was treated with triethylamine to give a mixture of the *cis*- and *trans*-isomers of 3-*O*-octadec-1′-enyl-D-glycerol 1,2-carbonate in which the *cis* isomer predominated. Alkaline hydrolysis of the carbonates gave a mixture of the *cis*- and *trans*-isomers of 1-*O*-octadec-1′-enyl-L-glycerol which was acylated with acetic anhydride or hexadecanoyl chloride in pyridine to give the diacetates or dipalmitates. The *cis*- and *trans*-isomers of the diacetates and dipalmitates were separated by t.l.c. on silica gel–silver nitrate plates. Alkaline hydrolysis of the *cis*-isomer of the diacetate gave the title compound.

We have previously [1] described routes for the preparation of 1-*O*-alk-1′-enylglycerols which are [2] suitable intermediates for the synthesis of plasmalogens and we now describe the development of one of these methods for the preparation of the title compound.

Other methods for the synthesis of 1-*O*-alk-1′-enylglycerols have been described recently. The first reported [3] method for the synthesis of the racemic compounds by the fission of 1,2-*O*-(2-bromoalkylidene)-glycerols with sodium in ether was later [4a] shown to give a mixture of the *cis*- and *trans*-isomers of both 1-*O*-alk-1′-enyl- and 2-*O*-alk-1′-enyl-glycerols. However, by using 1,3-*O*-(2-bromoalkylidene)glycerol as a starting material, Craig and Hamon [4b,c] showed that this was a convenient method for the preparation of a mixture of the *cis*- and *trans*-isomers of racemic 1-*O*-alk-1′-enylglycerols. Unfortunately this method is not suitable for the direct preparation of optically active material and the *trans*-isomer predominates in the product whereas the vinyl ether linkage in the plasmalogens has the *cis*-configuration.[5]

Preobrazhenskii and his co-workers [6a,b] have described the preparation of 1-*O*-alk-1′-enyl-2,3-*O*-isopropylideneglycerols from the corresponding acetylenic derivatives. This method will allow the direct preparation of optically active material and control over the configuration of the double bond but the authors have not described a method for the removal of the isopropylidene group to give a free 1-*O*-alk-1′-enylglycerol. However, Chacko [6c] claims that the isopropylidene group can be removed from 1-*O*-hexadec-1′-ynyl-2,3-*O*-isopropylideneglycerol with boric acid to give 1-*O*-hexadec-1′-ynylglycerol. 1-*O*-Alk-1′-enyl-2,3-*O*-isopropylideneglycerols have also been prepared [7] by the elimination of toluene-*p*-sulphonic acid from the toluene-*p*-sulphonate of 1-*O*-(2-hydroxyalkyl)-2,3-*O*-isopropylideneglycerol. However, in this reaction it seems probable that some 1-*O*-alk-2′-enyl-2,3-*O*-isopropylideneglycerol could be formed also. The same

[1] (*a*) J. Cunningham, R. Gigg, and C. D. Warren, *Tetrahedron Letters*, 1964, 1191; (*b*) J. Cunningham and R. Gigg, *J. Chem. Soc.*, 1965, 2968.

[2] A. J. Slotboom, G. H. de Haas, and L. L. M. van Deenen, *Chem. and Phys. Lipids*, 1967, **1**, 192.

[3] C. Piantadosi and A. F. Hirsch, *J. Pharm. Sci.*, 1961, **50**, 978; C. Piantadosi, A. F. Hirsch, C. L. Yarbro, and C. E. Anderson, *J. Org. Chem.*, 1963, **28**, 2425.

[4] (*a*) J. C. Craig, D. P. G. Hamon, H. W. Brewer, and H. Härle, *J. Org. Chem.*, 1965, **30**, 907; (*b*) J. C. Craig and D. P. G. Hamon, *Chem. and Ind.*, 1965, 1559; (*c*) *J. Org. Chem.*, 1965, **30**, 4168.

[5] W. T. Norton, E. L. Gottfried, and M. M. Rapport, *J. Lipid Res.*, 1962, **3**, 456; H. R. Warner and W. E. M. Lands, *J. Amer. Chem. Soc.*, 1963, **85**, 60.

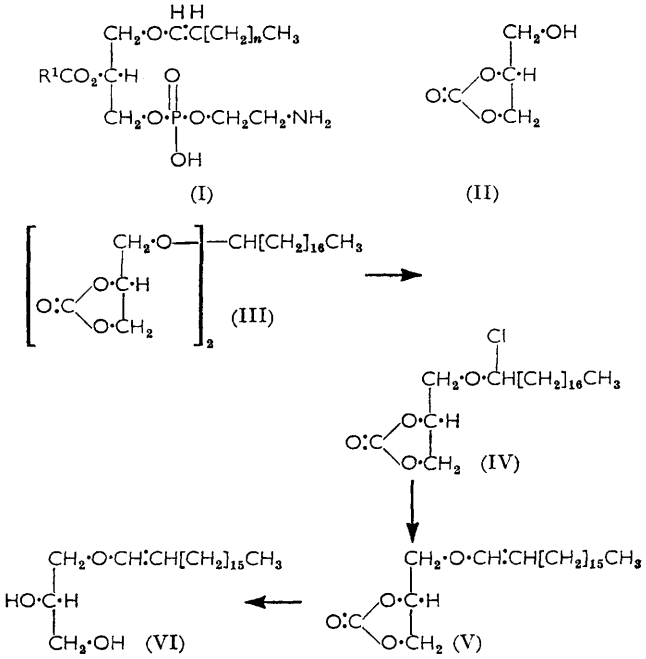
[6] (*a*) M. V. Berezovskaya, I. K. Sarycheva, and N. A. Preobrazhenskii, *Zhur. obshchei Khim.*, 1964, **34**, 543; (*b*) M. V. Berezovskaya, T. P. Zoobkova, I. K. Sarycheva, and N. A. Preobrazhenskii, *Zhur. org. Khim.*, 1966, **2**, 1774 (*Chem. Abs.*, 1967, **66**, 65,029); (*c*) G. K. Chacko, *Diss. Abs.*, 1967, **27**, *B*, 2290.

[7] E. A. Parfenov, G. A. Serebrennikova, and N. A. Preobrazhenskii, *Chem. Abs.*, 1966, **65**, 12102.

group of workers has also described [8a-c] a route to the 1-*O*-alk-1′-enyl-2,3-di-*O*-acylglycerols by elimination of ethanol from a 1-*O*-(1-ethoxyalkyl)2,3-di-*O*-acylglycerol or by elimination of a 1,2-di-*O*-acylglycerol from the di-(1,2-di-*O*-acylglycerol) acetal of a long-chain aldehyde. The elimination of ethanol from 1-*O*-(1-ethoxyhexadecyl)-2,3-di-*O*-palmitoylglycerol has also been used by Slotboom, de Haas, and van Deenen [2] for the preparation of racemic 1-*O*-hexadec-*trans*-1′-enyl-2,3-di-*O*-palmitoylglycerol. Ethyl hexadec-1-enyl ether was also produced owing to the elimination of 2,3-di-*O*-palmitoylglycerol from the starting material. The conditions of this reaction are vigorous (180°, acid catalysis) and the liberated 2,3-di-*O*-palmitoylglycerol would rapidly isomerise to an equilibrium mixture containing predominantly 1,3-di-*O*-palmitoylglycerol. Since an acid catalyst is present, some recombination of 1,3-di-*O*-palmitoylglycerol with the ethyl hexadec-1-enyl ether should occur and subsequent elimination of ethanol from the product would give 2-*O*-hexadec-1′-enyl-1,3-di-*O*-palmitoylglycerol. Slotboom *et al.*[2] did not completely characterise their product but treated it with pancreatic lipase to convert it into a 2-*O*-acyl-1-*O*-alk-1′-enylglycerol. Under these conditions any 1,3-di-*O*-acyl-2-*O*-alk-1′-enylglycerol would be degraded into 2-*O*-alk-1′-enylglycerol and this could explain why the racemic *trans*-plasmalogen which was synthesised from their product did not show positional isomerism. We have previously [1b] described a similar method involving the pyrolysis of the di(glycerol 1,2-carbonate) acetal of heptaldehyde at 200°. A mixture of *cis*- and *trans*-isomers was produced whereas the preparation of Slotboom *et al.*[2] contained only the *trans*-isomer.

Preobrazhenskii and his co-workers [9] have described a further route to 1-*O*-alk-1′-enylglycerols by the elimination of toluene-p-sulphonic acid from the toluene-p-sulphonate of 1-*O*-(2-hydroxyalkyl)-2,3-di-*O*-trimethylsilylglycerol by potassium t-butoxide. This method presumably gives a mixture of *cis*- and *trans*-isomers and it is possible that some 1-*O*-alk-2′-enylglycerol could be formed at the same time.

We previously [1b] investigated the reaction of acetyl chloride with heptaldehyde di(glycerol 1,2-carbonate) acetal. The product was 3-*O*-(1-chloroheptyl)glycerol 1,2-carbonate from which 3-*O*-hept-1′-enylglycerol 1,2-carbonate was obtained by the action of dry triethylamine. The *cis*- and *trans*-isomers of the latter compound were resolved by t.l.c. on silica gel and it was observed that the ratio of the two isomers produced in the pyrolysis method and in the chloro-ether method were different. We have subsequently shown that the chloro-ether route produces a preponderance of the *cis*-isomer whereas the pyrolysis method gives mainly the *trans*-isomer. The conditions of the chloro-ether route are very mild and since the *cis*-isomer was the major product and the method was suitable for the preparation of optically active material we have investigated this route for the preparation of the optically active long-chain 1-*O*-alk-1′-enylglycerols in detail.



The absolute configuration of the plasmalogen (I) had been determined previously [10] by comparison of the optical rotation of the D-glycerol 1-(ethanolamine phosphate), obtained from it by hydrolysis, with that of synthetic material. This configuration was confirmed [11] by optical rotatory dispersion studies on the 1-*O*-alk-1′-enylglycerol obtained from (I) by enzymic and chemical hydrolyses. Therefore for the synthesis of the required alkenyl ether by the chloro-ether route D-(glycerol 1,2-carbonate) (II) was required as an intermediate and a route to this compound was developed.[12] We have subsequently modified this procedure. Sodium borohydride (instead of lithium aluminium hydride) is now used for the preparation of methylenebis-2-*O*-(1-*O*-benzyl-L-glycerol) from the corresponding dialdehyde

[8] (*a*) E. N. Zvonkova, I. K. Sarycheva, and N. A. Preobrazhenskii, *Doklady Akad. Nauk. S.S.S.R.*, 1964, **159**, 1079 (*Chem. Abs.*, 1965, **62**, 11,680); (*b*) U.S.S.R.P., 165,710/1964 (*Chem. Abs.*, 1965, **62**, 6398); (*c*) T. V. Serebryakova, E. N. Zvonkova, G. A. Serebrennikova, and N. A. Preobrazhenskii, *Zhur. org. Khim.*, 1966, **2**, 2004 (*Chem. Abs.*, 1967, **66**, 85,405).

[9] (*a*) G. A. Serebrennikova, E. A. Parfenov, N. Y. Serebryakova, and N. A. Preobrazhenskii, *Khim. prirod Soedinenni*, 1966, 306; (*b*) E. A. Parfenov, G. A. Serebrennikova, S. Ya. Roumberz, and N. A. Preobrazhenskii, *Khim. prirod Soedinenni*, 1966, 367; (*c*) G. A. Serebrennikova, E. A. Parfanov, N. A. Perlova, and N. A. Preobrazhenskii, *Zhur. org. Khim.*, 1966, **2**, 1580 (*Chem. Abs.*, 1967, **66**, 65,028); (*d*) E. A. Parfenov, G. A. Serebrennikova, and N. A. Preobrazhenskii, *Zhur. org. Khim.*, 1966, **2**, 629, 633 (*Chem. Abs.*, 1966, **65**, 8747).

[10] S. J. Thannhauser, N. F. Boncoddo, and G. Schmidt, *J. Biol. Chem.*, 1951, **188**, 423; E. Baer and H. C. Stancer, *J. Amer. Chem. Soc.*, 1953, **75**, 4510.

[11] J. C. Craig, D. P. G. Hamon, K. K. Purushothaman, S. K. Roy, and W. E. M. Lands, *Tetrahedron*, 1966, **22**, 175. Cf. M.A. Grum-Grzhimailo, N. B. Karpova, L. V. Volkova, V. B. Korchagin, and N. A. Preobrazkenskii, *Zhur. org. Khim.*, 1966, **2**, 1187.

[12] J. Gigg and R. Gigg, *J. Chem. Soc.* (*C*), 1967, 1865.

since this procedure avoids the isolation of the dialdehyde.

The long-chain aldehydes (octadecanal and hexadecanal) required were prepared by oxidation of the methanesulphonates of the corresponding alcohols with dimethyl sulphoxide essentially as described previously.[13] Since these alcohols are now commercially available in high purity this represents a most convenient method for the preparation of the long-chain aldehydes. The crude aldehydes from the reaction mixture were converted directly to the dimethyl acetals which were purified from traces of alcohol and methanesulphonate by chromatography on alumina. At this stage the acetals were contaminated with small amounts of alkene but were sufficiently pure for the next stage of the reaction. The dimethyl acetals were allowed to react with racemic glycerol 1,2-carbonate [14] or D-(glycerol 1,2-carbonate) [12] (II) to give the corresponding racemic or optically active acetals (III) which were crystalline solids.

The reaction of acid chlorides with acetals was first investigated by Blaise [15] who showed that benzoyl chloride in the presence of magnesium or zinc iodides reacted with acetals to give benzoates of the corresponding alcohols. This reaction was further investigated by Post [16] who showed that benzoates and chloro-ethers were formed from acetals in refluxing benzoyl chloride in the absence of metallic iodides. Grummitt and Stearns [17] investigated the reaction of 3,5-dinitrobenzoyl chloride with acetals under various conditions and showed that at room temperature only one of the alkoxy-groups was replaced by chlorine to give an ester and a chloro-ether which was readily dehydrochlorinated to give a vinyl ether. A similar reaction has recently [18] been shown to occur between boron trichloride and acetals at −10°.

The reaction of excess of acetyl chloride with racemic heptanal di(glycerol 1,2-carbonate) acetal at reflux temperature caused a rapid conversion into a chloro-ether.[1b] The acetyl chloride acted as a convenient solvent which could be readily removed. With octadecanal di(glycerol 1,2-carbonate) acetal the reaction was slower and the product decomposed to a less polar compound on continued refluxing. Similar difficulties have been reported by Slotboom *et al.*[2] in the reaction of acetyl chloride with 1-*O*-(1-ethoxyhexadecyl)-2,3-di-*O*-palmitoylglycerol under these conditions. However by using an excess of acetyl chloride at room temperature for four days, high yields of the chloro-ether (IV) were obtained. The chloro-ether crystallised on evaporation of the excess of acetyl chloride and was then converted directly to the alkenyl ether (V) by the action of dry triethylamine. T.l.c., on silica gel, separated the *cis*- and *trans*-isomers of both the racemic and optically active 3-*O*-octadec-1′-enylglycerol 1,2-carbonates (V). The mixture of *cis*- and *trans*-isomers of compound (V) was reduced catalytically to give 3-*O*-octadecyl-D-glycerol 1,2-carbonate which had the same properties and an equal and opposite rotation to that of its enantiomer prepared as described below. Alkaline hydrolysis of compound (V) gave *cis*–*trans*-1-*O*-alk-1′-enyl-L-glycerol (VI). The isomers of this compound were not resolved by t.l.c. on silica gel but could be resolved on silica gel–silver nitrate [19] plates. The separation of the *cis*- and *trans*-isomers of simple vinyl ether by this technique has been described previously.[20] Dilute acid hydrolysis of compound (VI) showed complete hydrolysis to glycerol and octadecanal which was characterised as the 2,4-dinitrophenylhydrazone. Compound (VI) was also reduced catalytically to 1-*O*-octadecyl-L-glycerol with properties identical with those described previously.[21] The product was completely cleaved by sodium metaperiodate thus ruling out the presence of any 2-*O*-alk-1′-enylglycerol and the product of the cleavage was characterised as the 2,4-dinitrophenylhydrazone of the octadecyl ether of hydroxyacetaldehyde. The 1-*O*-octadecyl-L-glycerol was converted into the di-*p*-nitrobenzoate which had the same properties as described previously [21] and an equal and opposite rotation to that of its enantiomer prepared as described below. Compound (VI) was converted into the diacetate and catalytic reduction gave 1,2-di-*O*-acetyl-3-*O*-octadecyl-D-glycerol which had the same properties as reported previously [21] for this material.

The correct optical rotations obtained for the derivatives of 1-*O*-octadecyl-L-glycerol show that no racemisation had occurred during the conversion of D-(glycerol 1,2-carbonate) into 1-*O*-octadec-1′-enyl-L-glycerol.

For comparative purposes 1-*O*-octadecyl-D-glycerol was prepared as described previously [21] from octadecyl iodide and 1,2-*O*-isopropylidene-L-glycerol [22] and was converted into L-glycerol 1,2-carbonate, 1,2-di-*O*-acetate, and 1,2-di-*O*-*p*-nitrobenzoate.

A mixture of the *cis*- and *trans*-isomers of 1,2-di-*O*-hexadecanoyl-3-*O*-octadec-1′-enyl-D-glycerol was also prepared from compound (VI) and the *cis*- and *trans*-isomers of this compound as well as those of the corresponding diacetate were separated by preparative t.l.c. on silica gel–silver nitrate plates. The configurations of the two isomers were established by i.r. and confirmed by n.m.r. spectroscopy. The corresponding spectra of the *cis*- and *trans*-isomers of racemic 1-*O*-hexadec-1′-enylglycerol and its diacetate have been described previously.[2,4c] We subsequently found that the *cis*-dipalmitate could be obtained almost free from the *trans*-isomer by repeated recrystallisation of the mixed isomers from light petroleum.

[13] V. Mahadevan, F. Phillips, and W. O. Lundberg, *Lipids*, 1966, **1**, 183.
[14] J. Cunningham and R. Gigg, *J. Chem. Soc.*, 1965, 1553.
[15] E. E. Blaise, *Compt. rend.*, 1904, **139**, 1211; 1905, **140**, 661.
[16] H. W. Post, *J. Org. Chem.*, 1936, **1**, 231.
[17] O. Grummitt and J. A. Stearns, *J. Amer. Chem. Soc.*, 1955, **77**, 3136.
[18] D. K. Black and S. R. Landor, *J. Chem. Soc.*, 1965, 5225.
[19] L. J. Morris, *J. Lipid Res.*, 1966, **7**, 717.
[20] E. N. Zvonkova, G. A. Anan'eva, M. A. Belonsova, I. K. Sarycheva, and N. A. Preobrazhenskii, *Chem. Abs.*, 1966, **65**, 8746.
[21] E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, 1941, **140**, 397.
[22] J. LeCocq and C. E. Ballou, *Biochemistry*, 1964, **3**, 976.

Alkaline hydrolysis of the acetate of the *cis*-isomer gave 1-*O*-octadec-*cis*-1′-enyl-L-glycerol, which had an i.r. spectrum identical with that described [5] previously for the alkenyl ether obtained from the natural plasmalogen. 1-*O*-Octadec-*trans*-1′-enyl-L-glycerol was obtained from the *trans*-diacetate and the i.r. spectrum was also characteristic of a *trans*-alkenyl ether [5] showing strong absorption at 1150—1250 and 944 cm.$^{-1}$.

EXPERIMENTAL

Thin-layer chromatography was carried out as described previously.[1b] The light petroleum used had b. p. 40—60°. Solvents were evaporated under reduced pressure. Specific rotations were measured at 22—24° on a Bendix Automatic Polarimeter. N.m.r. spectra were taken in deuteriochloroform (reference, tetramethylsilane) on a Varian A 60 spectrometer.

Octadecanal Dimethyl Acetal.—Sodium hydrogen carbonate (43 g.) and n-octadecyl methanesulphonate [23] (56 g.) [prepared from n-octadecanol (B.D.H. Ltd., ' not less than 99% by g.l.c. ')] in dimethyl sulphoxide (225 ml.) were stirred vigorously at 150° for 20 min., cooled, and poured into ice–water. The precipitated solid was collected and washed thoroughly with water. After drying, the crude aldehyde was heated under reflux in dry methanol (500 ml.) containing toluene-*p*-sulphonic acid (2 g.) for 3 hr. The acid was neutralised by stirring with an excess of potassium carbonate, the solvent evaporated, and the residue extracted with ether. The extract was dried and the solvent evaporated to give the crude dimethyl acetal (42 g.). T.l.c. [ether–light petroleum (1 : 3) as mobile phase] showed the acetal (R_F 0·9) and traces of olefin (R_F 0·95), alcohol (R_F 0·3), and methanesulphonate (R_F 0·46). The product was filtered through an alumina column (8 × 10 cm.) in ether–light petroleum (1 : 5) to give the dimethyl acetal (30 g.) still contaminated with the trace of olefin but free from alcohol and methanesulphonate. A small sample was distilled for analysis, b. p. 147°/0·3 mm., n_D^{20} 1·4420 (Found: C, 76·1; H, 13·2. Calc. for $C_{20}H_{42}O_2$: C, 76·4; H, 13·5%) (lit.,[24] b. p. 162—167°/0·5 mm., n_D^{25} 1·4410).

n-Hexadecanal dimethyl acetal [24] was prepared in a similar way from n-hexadecanol (B.D.H. Ltd., ' not less than 99% by g.l.c.').

Di(glycerol 1,2-Carbonate) Acetals of Aldehydes.—Octadecanal dimethyl acetal (8·3 g.), racemic glycerol 1,2-carbonate [14] (6·2 g.), and toluene-*p*-sulphonic acid (10 mg.) in dry benzene (120 ml.) were heated under reflux with stirring and the solvent was allowed to distil slowly from the mixture to remove the methanol formed. The volume of the solution was maintained by the occasional addition of portions of dry benzene. After 2 hr., the solution was diluted with dry ethyl acetate (100 ml.) and washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated. The residue was recrystallised from cyclohexane to give racemic octadecanal di(glycerol 1,2-carbonate) acetal (10 g.), m. p. 76—78° (Found: C, 63·9; H, 9·2. Calc. for $C_{26}H_{46}O_8$: C, 64·2; H, 9·5%).

In the same way racemic hexadecanal di(glycerol 1,2-carbonate) acetal was prepared from hexadecanal dimethyl acetal and racemic glycerol 1,2-carbonate, m. p. 72—75° (Found: C, 63·2; H, 9·05. Calc. for $C_{24}H_{42}O_8$: C, 63·0; H, 9·2%) and *octadecanal di*(D-*glycerol 1,2-carbonate*) *acetal* (III) was prepared from octadecanal dimethyl acetal and D-(glycerol 1,2-carbonate),[12] m. p. 86—87°, $[\alpha]_D$ +14·5° (*c* 1 in $CHCl_3$) (Found: C, 64·15; H, 9·4. $C_{26}H_{46}O_8$ requires C, 64·2; H, 9·5%).

1-*O*-*Benzyl*-L-*glycerol.*—1,6-Di-*O*-benzyl-2,5-*O*-methylene-D-mannitol [12] (24 g.) in 20% aqueous methanol (300 ml.) was added to sodium metaperiodate (17 g.) in 20% aqueous methanol (300 ml.). After 1 hr. at room temperature the solution was filtered, the filtrate cooled to 5°, and sodium borohydride (5 g.) was added. After 2 hr., the solution was acidified with glacial acetic acid and evaporated to remove the methanol. The aqueous residue was extracted with chloroform and the extract was washed with aqueous sodium thiosulphate to remove a trace of iodine, dried ($MgSO_4$), and evaporated. The residue was treated with N-methanolic hydrogen chloride solution (200 ml.) for 2 hr. at room temperature and the acid neutralised with an excess of potassium carbonate. The solvent was evaporated and the residue was extracted with chloroform. Evaporation of the solvent and distillation gave 1-*O*-benzyl-L-glycerol (19·5 g.), b. p. 125°/0·5 mm., α_D −7° (1 dm., pure substance) [lit.,[12] α_D −6·5° (1 dm., pure substance), b. p. 125°/0·5 mm.].

Racemic cis–trans-1-O-*Octadec*-1′-*enylglycerol.*—Racemic octadecanal di(glycerol 1,2-carbonate) acetal (5 g.) was dissolved in freshly distilled acetyl chloride (50 ml.) and the solution was kept at 22° for 4 days. The acetyl chloride was evaporated under anhydrous conditions and the solid residue was refluxed with dry freshly distilled triethylamine (50 ml.) for 15 min. under anhydrous conditions. The mixture was poured into dry ether (200 ml.) and the triethylamine hydrochloride was removed by filtration. The filtrate was evaporated to dryness to give crude racemic *cis–trans*-3-O-octadec-1′-enylglycerol 1,2-carbonate. T.l.c. (ether as mobile phase) showed the carbonates (R_F 0·7 and 0·8) with the isomer (R_F 0·7) predominant, traces of impurity at the origin and the solvent front, and 3-*O*-acetylglycerol 1,2-carbonate [1b] (R_F 0·3). The crude product was refluxed for 15 min. in a mixture of methanol (100 ml.) and 50% (w/v) aqueous potassium hydroxide (4 ml.) and the methanol evaporated. The residue was extracted with ether and the extract washed with saturated aqueous potassium chloride, dried ($MgSO_4$), and evaporated. Crystallisation of the residue from light petroleum gave racemic *cis–trans*-1-*O*-octadec-1′-enylglycerol, (2·3 g.), m. p. 50—53°, $\nu_{max.}$ 1665 cm.$^{-1}$ (−O−CH=CH−) (Found: C, 73·6; H, 12·2. Calc. for $C_{21}H_{42}O_3$: C, 73·6; H, 12·4%). T.l.c. on silica gel–silver nitrate (10 : 1) plates showed the two isomers (R_F 0·6 and 0–7, ether as mobile phase).

The 1-*O*-octadec-1′-enylglycerol (250 mg.) in ethanol with sodium hydrogen carbonate (25 mg.) was treated with hydrogen in the presence of platinum oxide until uptake was complete. After filtration and evaporation of the solvent, the residue was crystallised from cyclohexane to give 1-*O*-octadecylglycerol (220 mg.), m. p. 66—68° (lit.,[21] m. p. 71—71·5°). The product (70 mg.) was treated with sodium metaperiodate (100 mg.) in 20% aqueous methanol (30 ml.). After 1 hr., t.l.c. (ether as mobile phase) showed complete conversion of the starting material (R_F 0·5) into a product (R_F 0·9). The methanol was evaporated and the residue extracted with ether and the extract evaporated.

[23] W. J. Baumann and H. K. Mangold, *J. Org. Chem.*, 1964, **29**, 3055.

[24] F. Leupold and H. Büttner, *Z. physiol. Chem.*, 1952, **291**, 178.

The octadecyl ether of hydroxyacetaldehyde was converted into the 2,4-dinitrophenylhydrazone, m. p. 79—81° (lit.,[25] 73°) (Found: C, 63·5; H, 9·5; N, 11·4. Calc. for $C_{26}H_{44}N_4O_5$: C, 63·4; H, 9·0; N, 11·4%).

1-*O*-Octadec-1′-enylglycerol was treated with 2,4-dinitrophenylhydrazine hydrochloride in ethanol. The precipitated 2,4-dinitrophenylhydrazone of octadecanal was recrystallised from ethanol, m. p. and mixed m. p. 104—106° (lit.,[13] 108—109°).

3-O-*Octadecyl*-D-*glycerol* 1,2-*Carbonate*.—Octadecanal di-D-(glycerol 1,2-carbonate) acetal was converted into 3-*O*-octadec-1′-enyl-D-glycerol 1,2-carbonate as described for the racemic compound. The crude product was reduced with hydrogen in the presence of platinum oxide in a mixture of ethanol and ethyl acetate until uptake was complete. The solvents were evaporated and the *product* was washed with water to remove 3-*O*-acetylglycerol 1,2-carbonate, dried, and recrystallised from methanol and light petroleum, m. p. 58—60°, $[\alpha]_D$ +5·5° (*c* 2 in $CHCl_3$) (Found: C, 71·2; H, 11·0. $C_{22}H_{42}O_4$ requires C, 71·3; H, 11·4%) (for the enantiomer see below).

cis–trans-1-O-*Octadec*-1′-*enyl*-L-*glycerol*.—Octadecanal di-D-(glycerol 1,2-carbonate) acetal was converted into the *product* as described above for the racemic compound. Yield 80%, m. p. 54—55°, $\nu_{max.}$ 1668 $cm.^{-1}$ (–O–CH=CH–) (Found: C, 73·8; H, 12·1. $C_{21}H_{42}O_3$ requires C, 73·6; H, 12·4%).

1-O-*Octadecyl*-L-*glycerol*.—1-*O*-Octadec-1′-enyl-L-glycerol (200 mg.) was reduced as described for the racemic compound. The product was recrystallised from light petroleum to give 1-*O*-octadecyl-L-glycerol (150 mg.), m. p. 70—72°, $[\alpha]_D$ +1·5° (*c* 1 in $CHCl_3$) (Found: C, 73·3; H, 12·7. Calc. for $C_{21}H_{44}O_3$: C, 73·2; H, 12·9%) [lit.,[21] m. p. 71—72°, $[\alpha]_D$ +4° (*c* 1 in $CHCl_3$)]. The compound was converted into the di-*p*-nitrobenzoate, m. p. 64—66°, $[\alpha]_D$ –31·2° (*c* 1 in $CHCl_3$) (Found: C, 65·5; H, 7·7; N, 4·5. Calc. for $C_{35}H_{50}N_2O_9$: C, 65·4; H, 7·8; N, 4·4%) [lit.,[21] m. p. 65·5—66·5°, $[\alpha]_D$ –27·9° (*c* 7·8 in $CHCl_3$)] (for the enantiomer see below).

1,2-*Di*-O-*acetyl*-3-O-*octadecyl*-D-*glycerol*.— *cis–trans*-1-*O*-octadec-1′-enyl-L-glycerol was acetylated with acetic anhydride in pyridine and the diacetate was obtained as a semi-crystalline solid. T.l.c. on silica gel–silver nitrate (10 : 1) plates showed the separation of the two isomers [R_F 0·55 and 0·65, ether–light petroleum (1 : 2) as mobile phase]. A portion of the mixture of isomers was reduced as described above and the product was distilled at 200° (bath)/0·05 mm. to give 1,2-di-*O*-acetyl-3-*O*-octadecyl-D-glycerol as a waxy solid, m. p. 32—34° $[\alpha]_D$ –6·3° (*c* 2 in $CHCl_3$) (Found: C,70·0; H, 10·9. Calc. for $C_{25}H_{48}O_5$: C, 70·0; H, 11·3%) [lit.,[21] b. p. 180—183°/10^{-3} mm. m. p.s 34—34·5 and 42—43°, $[\alpha]_D$ –7·6° (*c* 12·6 in $CHCl_3$)] (for the enantiomer see below).

Separation of the cis- *and* trans-*Isomers of* 1,2-*Di*-O-*acetyl*-3-O-*octadec*-1′-*enyl*-D-*glycerol*.—The mixture of *cis*- and *trans*-isomers prepared above (150 mg.) was applied as a streak and chromatographed on a silica gel–silver nitrate (4 : 1) plate (20 × 20 × 0·2 cm.) using ether–light petroleum (1 : 4) as solvent. A small strip of the plate was sprayed with alkaline potassium permanganate solution [1b] to show the positions of the two isomers and the stationary phase containing these was scraped off and eluted with ether. The faster-moving trans-*isomer* (38 mg.) had m. p. 51—52°, $\nu_{max.}$ 1677, 1660 (*trans* –O–CH=CH–) and 925 $cm.^{-1}$ (*trans* –CH=CH–), $[\alpha]_D$ –12·7° (*c* 1 in $CHCl_3$) (Found: C, 70·3; H, 10·7. $C_{25}H_{46}O_5$ requires C, 70·4; H, 10·9%). The slower-moving cis-*isomer* (75 mg.) had m. p. 23—25°, $\nu_{max.}$ 1665 $cm.^{-1}$ (*cis* –O–CH=CH–), $[\alpha]_D$ –6·7° (*c* 1 in ethanol) (Found: C, 70·3; H, 11·1%).

cis- and trans-*Isomers of Racemic* 1-O-*Octadec*-1′-*enyl*-2,3-*di*-O-*palmitoylglycerol*.—Hexadecanoyl chloride (4·8 g.) (prepared from palmitic acid, B.D.H. Ltd., ' not less than 98% by g.lc.') in dry carbon tetrachloride (10 ml.) was added slowly to a stirred solution of racemic 1-*O*-octadec-1′-enylglycerol (2 g.) in dry carbon tetrachloride (25 ml.) and dry pyridine (3 ml.) at 5° and the mixture was left overnight at room temperature. The mixture was washed with water, saturated aqueous sodium hydrogen carbonate, and water, dried ($MgSO_4$), and evaporated. The crude product was chromatographed on neutral alumina, eluting with light petroleum and ether–light petroleum (1 : 10) and the product was recrystallised from acetone to give the dipalmitate (3·65 g.) as needles, m. p. 53—55°. T.l.c. on silica gel–silver nitrate plates [ether–light petroleum (1 : 9) as mobile phase] showed the *cis*- and *trans*-isomers at R_F 0·53 and 0·64. Preparative t.l.c., as described above for the diacetates, of 150 mg. of the mixed isomers [ether–light petroleum (1 : 9) as mobile phase] gave two fractions which were recrystallised from acetone. The faster-moving compound (R_F 0·64) (36 mg.), had m. p. 56—57° (Found: C, 77·7; H, 12·3. Calc. for $C_{53}H_{102}O_5$: C, 77·7; H, 12·5%). The slower-moving compound (R_F 0·53) (80 mg.), had m. p 50—52° (Found: C, 77·3; H, 12·1%).

cis- *and* trans-*Isomers of* 1-O-*Octadec*-1′-*enyl*-2,3-*di*-O-*palmitoyl*-L-*glycerol*.—The mixture of *cis*- and *trans*-isomers of this compound were prepared as described above for the racemic compound starting from 1-*O*-octadec-1′-enyl-L-glycerol (Found: C, 77·7; H, 12·2%). Preparative t.l.c., as described above for the racemic compound, separated the cis-*isomer* (slower-moving compound), m. p. 56—58°, $\nu_{max.}$ 1665 (*cis* –O–CH=CH–) and 734 $cm.^{-1}$ (*cis* –CH=CH–), $[\alpha]_D$ –2·9° (*c* 0·6 in $CHCl_3$), n.m.r. doublet at δ 5·96 p.p.m. (J = 6·2 c./sec.) (olefinic H on C-1′) (Found: C, 77·6; H, 12·3%) [lit.,[4c] doublet at δ 5·87 p.p.m. (J = 6·5 c./sec.) for synthetic racemic 1,2-di-*O*-acetyl-3-*O*-hexadec-*cis*-1′-enylglycerol; lit.,[2] doublet at δ 5·93 p.p.m. (J = 6·5 c./sec.) for natural 1,2-di-*O*-acetyl-3-*O*-alk-*cis*-1′-enylglycerol]. The trans-*isomer* (faster-moving compound) had m. p. 47—49°, $\nu_{max.}$ 1675, 1660 (*trans* –O–CH=CH–) and 925 $cm.^{-1}$ (*trans* –CH=CH–), n.m.r. doublet at δ 6·29 p.p.m. (J = 12·5 c./sec.) (olefinic H on C-1′) [lit.,[4c] doublet at δ 6·20 p.p.m. (J = 12·5 c./sec.) and lit.,[2] δ 6·28 p.p.m. (J = 12·5 c./sec.) for synthetic 1,2-di-*O*-acetyl-3-*O*-hexadec-*trans*-1′-enylglycerol].

The *cis*-dipalmitate (440 mg.) was obtained almost free from the *trans*-isomer after two recrystallisations of the mixed isomers (1 g.) from light petroleum (100 ml.) at 0°.

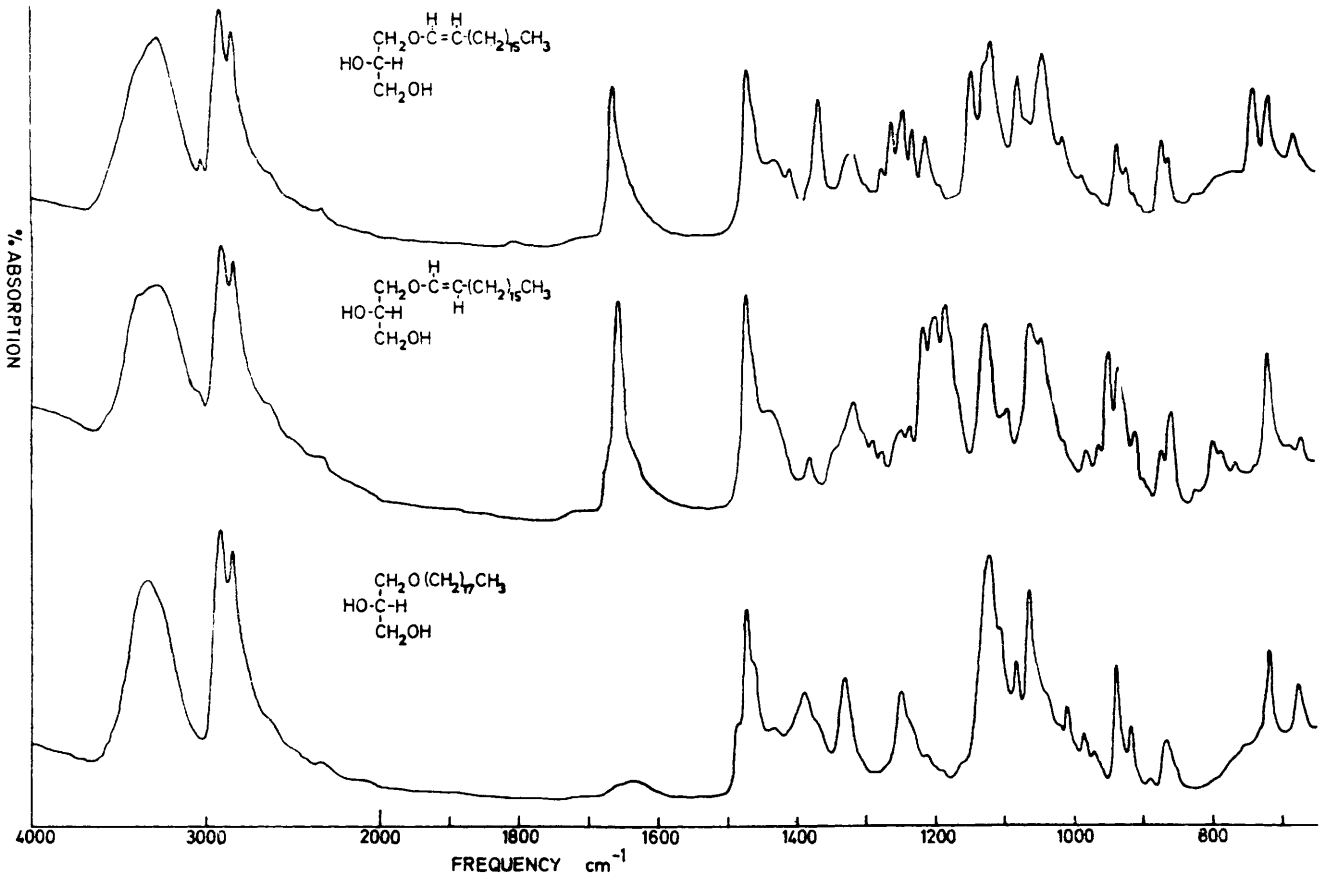
1-O-*Octadecyl*-2,3-*di*-O-*palmitoyl*-L-*glycerol*.— Catalytic hydrogenation of the mixture of isomers of the dipalmitate and recrystallisation from acetone gave the *product*, m. p. 57—59°, $[\alpha]_D$ –4° (*c* 2 in $CHCl_3$) (Found: C, 77·5; H, 12·6. $C_{53}H_{104}O_5$ requires C, 77·5; H, 12·8%).

cis- *and* trans-1-O-*Octadec*-1′-*enyl*-L-*glycerol*.—1,2-Di-*O*-acetyl-3-*O*-octadec-*cis*-1′-enyl-D-glycerol was hydrolysed with ethanolic potassium hydroxide and the 1-O-*octadec*-cis-1′-*enyl*-L-*glycerol* was recrystallised from light petroleum, m. p. 55—56°, $[\alpha]_D$ –2° (*c* 2 in $CHCl_3$) (Found: C, 73·5; H, 12·5. $C_{21}H_{42}O_3$ requires C, 73·6; H, 12·4%).

[25] W. H. Davies, I. M. Heilbron, and W. E. Jones, *J. Chem. Soc.*, 1933, 165.

The corresponding *trans*-diacetate was hydrolysed to give 1-O-*octadec*-trans-1′-*enyl*-L-*glycerol*, m. p. 68—69°, $[\alpha]_D$ −3·4° (*c* 1·8 in $CHCl_3$) (Found: C, 73·2; H, 12·1%).

The i.r. spectra (in KBr discs) of these two compounds together with that of 1-*O*-octadecyl-L-glycerol are shown in the Figure. The spectrum of the 1-*O*-alk-1′-enyl-L-glycerol obtained from natural plasmalogens has been published.[5]



3-O-*Octadecyl*-L-*glycerol* 1,2-*Carbonate*.—1-*O*-Octadecyl-D glycerol was prepared from 1,2-*O*-isopropylidene-L-glycerol [23] and octadecyl iodide (prepared from octadecyl methanesulphonate and sodium iodide) as described previously,[21] m. p. 70—71°, $[\alpha]_D$ −2° (*c* 0·8 in $CHCl_3$) (Found: C, 73·1; H, 12·6. Calc. for $C_{21}H_{44}O_3$: C, 73·2; H, 12·9%) [lit.,[21] $[\alpha]_D$ −2·3° (*c* 1·1 in $CHCl_3$), m. p. 71—72°]. The diacetate had $[\alpha]_D$ +7·3° (*c* 1·95 in $CHCl_3$) (Found: C, 70·2; H, 11·2. Calc. for $C_{25}H_{48}O_5$: C, 70·1; H, 11·3%) [lit.,[21] $[\alpha]_D$ +7·6° (*c* 11·21 in $CHCl_3$)]. The di-*p*-nitrobenzoate, m. p. 64—66°, $[\alpha]_D$ +31° (*c* 1 in $CHCl_3$) (Found: C, 65·7; H, 7·9; N, 4·5. Calc. for $C_{35}H_{50}N_2O_9$: C, 65·4; H, 7·8; N, 4·4%) [lit.,[21] m. p. 66·5—67°, $[\alpha]_D$ +29·1° (*c* 6·7 in tetrachloroethane)].

The *carbonate*, prepared by the action of phosgene in pyridine, had m. p. 59—60°, $[\alpha]_D$ −5·6° (*c* 1·9 in $CHCl_3$) (Found: C, 71·0; H, 11·1. $C_{22}H_{42}O_4$ requires C, 71·3; H, 11·4%).

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